IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AUXILIUM PHARMACEUTICALS, INC. and FCB I, LLC, Plaintiffs, v. UPSHER-SMITH LABORATORIES, INC., Defendant.	C.A. No. 13-148-SLR **PUBLIC VERSION**

DEFENDANT UPSHER-SMITH LABORATORIES, INC.'S REPLY BRIEF IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT OF NON-INFRINGEMENT OF THE PATENTS-IN-SUIT

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INTRODUCTION

A disclaimer of equivalents can occur on any of three bases: (i) an explicit definition of what the invention "is"; (ii) a distinction over prior art by a specific limitation; and (iii) disparagement of prior art. The patentee in this case did all three by distinguishing the added limitation of specific Hsieh enhancers from the non-Hsieh enhancers in the prior art and disparaging the very enhancers now accused of being equivalent. The patentee cannot now recapture non-Hsieh enhancers, regardless of unforeseeability or tangentiality. The patentee cannot dispute the disclaimers in the specification and file history – the intrinsic record – by providing subjective evidence not available to the public. Because of the explicit disclaimers, the issue of non-infringement is a matter of law appropriate for summary judgment.

The patent system rewards inventors only for what they invented, and not for the innovations of others. Auxilium[1] does not dispute that the patents-in-suit claim only a combination of testosterone with at least one of five specific macrocyclic compounds. Auxilium cannot genuinely dispute that the Applicant, not the Examiner, defined the patent claims by distinguishing these five macrocyclic Hsieh enhancers from combinations of testosterone with other known "enhancers" described in Dudley (U.S. Patent No. 6,503,894). When a patentee amends the claims and makes explicit statements that the claimed invention is different from the prior art, the patentee is estopped from asserting that such distinguished features of the prior art are equivalent to the added limitation. *Augustine Med., Inc. v. Gaymar Indus. Inc.*, 181 F.3d 1291, 1299 (Fed. Cir. 1999). As a matter of law, Auxilium surrendered "non-Hsieh" enhancers including the enhancers disclosed in Dudley, whether used individually or in combination.

[1] "Auxilium" refers collectively to Plaintiffs.

The parties agree on the following facts:

- Each of the patents-in-suit is based on the same application and shares the same specification. D.I. 40 at 6-7.[2]
- The common specification states that "the enhancer of the present invention is" a macrocyclic Hsieh enhancer. D.I. 1, Ex. A at col. 6, l. 23- col. 7, l. 1.
- The applicant amended the claims during prosecution of the parent patent to recite the specific macrocyclic enhancer Oxa-2-one, in the face of the obviousness rejection over the Dudley and Hsieh reference. D.I. 40 at 7-9.
- The applicant expressly distinguished its claims from Dudley noting, among other things, that the combination of a Hsieh enhancer with testosterone was not found in the prior art. D.I. 34-1 at 24-25; D.I. 56-8 at USL0003587; D.I. 57-1 at CPEX 0114513; D.I. 57-6 at CPEX0114853; D.I. 58-1 at CPEX0116245; D.I. 58-7 at CPEX0115202; D.I. 58-15 at CPEX 0115538; D.I. 59-2 at CPEX0115888; D.I. 59-9 at USL00454371-72; D.I. 60-2 at AUXSJ00001420-21; D.I. 60-11 at AUXSJ00001009-10.
- Each issued claim of the patents recites only one or a few specific Hsieh enhancers (D.I. 40 at 2), which are cyclic enhancers. D.I. 50 ¶¶ 131-33.
- USL's[3] formulation contains no Hsieh enhancer (D.I. 40 at 11, 15), nor cyclic enhancers. D.I. 40 at 15 (citing D.I. 50 ¶¶ 165-67).
- The ingredients in USL's accused "enhancer system" are individually and specifically disclosed in Dudley. D.I. 40 at 19.
- The acknowledged prior art teaches combining enhancers. *see below* at p. 15; D.I. 1, Ex. A-J; *see also,* D.I. 40 at 20 (citing D.I. 51 ¶¶ 136-138).
- The specification of the patents-in-suit criticizes formulas that use enhancers disclosed in the Dudley reference for, among other reasons, causing skin irritation. D.I. 1, Ex. A at col. 3, ll. 51-63.
- Hsieh enhancers differ from other penetration enhancers by their distinctive chemical structure. D.I. 40 at 6.

These facts are material and dispositive. Auxilium does not dispute that there is no literal infringement. Basic limits on the doctrine of equivalents preclude a finding of equivalency in this case. The doctrine of equivalents is narrow, and reserved for insubstantial differences between

[2] For ease of reference, citations are to the '968 patent (the parent patent) specification which is substantially identical to the specification of all of the patents-in-suit.

[3] "USL" refers to Defendants Upsher-Smith Laboratories, Inc.

the invention as claimed and the alleged equivalent. *See Butamax Adv. Biofuels LLC. v. Gevo, Inc.*, No. 11-54-SLR, 2013 WL 1137182, at *13 (D. Del. Mar. 19, 2013) (citing *Zelinski v. Brunswick Corp.*, 185 F.3d 1311, 1316 (Fed. Cir. 1999)). Auxilium repeatedly argues that USL's formulation is surprising and was not foreseen by Auxilium or predictable based on Auxilium's work. *See, e.g.*, D.I. 40 at 10-11, 21-22. The doctrine of equivalents cannot be used to expand one's patent claims to capture the inventive work of others. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 493 F.3d 1368, 1379 (Fed. Cir. 2007) ("Festo XIII") ("The theory of the doctrine of equivalents is that an applicant through the doctrine of equivalents should only be able to protect the scope of his invention, not to expand the protectable scope of the claimed invention to cover a new and unclaimed invention." (internal citation omitted)).

Moreover, the specification, prosecution history and the claims – as the public record on which competitors are entitled to rely – clearly identified the boundaries of Auxilium's property rights. After narrowly describing the invention as containing a Hsieh enhancer, narrowly claiming the invention, and narrowing the scope of the patent by distinguishing the Dudley enhancers, Auxilium cannot recapture the surrendered subject matter.

ARGUMENT

Prior to filing the initial application for the patents-in-suit, named inventor Gyurik faced a landscape of known testosterone gels and penetration enhancers. D.I. 40 at 5-6. In short, Gyurik was not the first to invent testosterone gels, and was not the first to invent testosterone gels with penetration enhancers. Gyurik was trying to improve known testosterone gel formulations like those disclosed in the Dudley patent and a commercial embodiment, ANDROGEL®. *Id.* Auxilium alleges he then "developed a testosterone gel formulation containing a Hsieh enhancer." D.I. 40 at 6.

Gyurik initially attempted to patent a testosterone gel with all of the Hsieh enhancers. D.I. 56-1 at USL0002822 (Claim 40). Yet, in the face of the Dudley disclosure and the teachings of the Hsieh patent (U.S. Patent No. 5,023,252), Gyurik has only been allowed claims reciting specific Hsieh enhancers he specifically tested, and which showed unexpected results. As indicated in the specification and throughout the prosecution history, Gyurik criticized and distinguished the Dudley enhancers. Auxilium cannot now take back what Gyurik clearly distinguished and therefore gave up during prosecution, and what was never part of his invention.

Subsequent to Gyurik's work, USL turned its attention to solving the problem of low delivery of testosterone through the skin. USL surveyed the landscape of known testosterone gels and penetration enhancers (including the published Gyurik patent application and the Dudley patent) and created its own testosterone gel, which Auxilium now recognizes as novel. USL's formulation contains ingredients that Gyurik clearly identified as not part of his invention by explicit arguments and disparagement, and by narrow claiming. Auxilium cannot capture USL's formulation, which lacks a Hsieh enhancer, and which Gyurik did not invent.

I. The material facts are undisputed and dispositive: Auxilium disclaimed the non-Hsieh compounds in USL's formula.

The Federal Circuit, building on Supreme Court precedent, has clearly established that when a patent specification, file history, and claim amendments distinguish patent claims over prior art, the patentee cannot use the doctrine of equivalents to broaden the amended limitation back into the prior art it criticized. "After adding a claim limitation during prosecution to overcome prior art, the applicant cannot later assert that the distinguished feature of the prior art is equivalent to the added limitation." *Augustine Med.*, 181 F.3d at 1299. Auxilium cannot now

assert that the distinguished features of the prior art, namely the non-cyclic Dudley enhancers, are equivalent to any or all of the five specific macrocyclic Hsieh enhancers. *Id.*

Auxilium cannot avoid the effect of its distinctions and amendments by claiming that USL's combination of known enhancers was surprising and unforeseeable. First, foreseeability has no role when it comes to a clear disclaimer like the one in this case. *Conoco, Inc. v. Energy & Envtl. Int'l, L.C.*, 460 F.3d 1349, 1363-65 (Fed. Cir. 2006) (noting that there are different tests for estoppel). Auxilium distinguished and disclaimed the enhancers of Dudley from the Hsieh enhancers, and never limited its disclaimer to the use of individual Dudley enhancers as opposed to combinations. Second, an equivalent need only be known to exist to be foreseeable, it need not be known to be suitable for the claimed invention. *Festo XIII,* 493 F.3d at 1382 ("An equivalent is foreseeable if one skilled in the art would have known that the alternative existed in the field of art as defined by the original claim scope, even if the suitability of the alternative for the particular purposes defined by the amended claim scope were unknown."). Here, each of the three accused equivalents and the combination of them was foreseeable as a matter of law because they are disclosed in the prior art. D.I. 40 at 19. Where the alleged equivalent is unforeseen and surprising, as Auxilium itself argues, the Federal Circuit has made it clear that the doctrine of equivalents should rarely if ever be used to capture such an equivalent that is "non-obvious." *Festo XIII,* 493 F.3d at 1379-80.

A. Auxilium has only been allowed claims reciting one of five specific closely related macrocyclic Hsieh enhancers for which it demonstrated surprising results.

Despite numerous attempts to secure broader claims, Auxilium has only been able to get claims to testosterone gel formulations with a subset of five tested Hsieh enhancers. Of 94 claims issued to Auxilium to date, every single one recites, and has been required by the Patent Office to recite, one or more of the five specific macrocyclic enhancers. The patent claims in the

original application recited "an androgen, a Hsieh enhancer, and a thickening agent." D.I. 56-1 at USL0002822; D.I. 50 ¶ 134. Each time it was presented, this broad combination faced an obviousness rejection based on Dudley. *See, e.g.,* D.I. 56-8 at USL0003542-47; D.I. 57-2 at CPEX0114646-48; D.I. 57-10 at CPEX0114988-90; D.I. 58-3 at CPEX0116370-72; D.I. 58-10 at CPEX0115321-23; D.I. 58-18 at CPEX0115665-67; D.I. 59-5 at CPEX0116013-15; D.I. 59-11 at USL00453963-72; D.I. 60-2 at AUXSJ00001498-1501; D.I. 60-8 at AUXSJ00000896-901.

During prosecution of the '518 patent, the Applicant made the same incorrect argument as Auxilium now makes in litigation – that the claims of the '968 patent were amended to "align the scope" with the unexpected results that demonstrated that TESTIM produced a 30% greater mean "area under the curve" than ANDROGEL®. D.I. 40 at 24-25; D.I. 50 ¶¶ 209-212; D.I. 60-11 at AUXSJ00001011-12. The Examiner rejected this characterization outright, noting that the claims were allowed because of the specific ingredients claimed. The Examiner stated:

> It is noted merely for clarity of record that the statement by the Applicant that in the parent application of 10/473724 now U.S. Pat. No. 7320968, that the 30% increase of the AUC_{0-24} and C_{max} was unexpected to the Androgel® leading to issuance, is not entirely correct. I was the examiner on the parent and the improved therapeutic profile was a very serious consideration as to the benefits of the specific composition in the patented claims, but so was the inclusion of eight different components present in the claimed patent for the particular method of use where the art of record did not disclose the specific combination of eight specific components in the recited amounts for the specific use claimed; where the combination of these considerations together determined patentability.
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> D.I. 60-14 at AUXSJ00001195 (emphasis added); *compare* D.I. 60-14 at AUXSJ00001203-04 (Applicant agreed with the Examiner amending his claim to conform to the same structure).

This clear history and clear statement of the patent examiner is persuasive evidence that the Hsieh enhancers are critical to the claimed invention. *Glaxo Wellcome, Inc. v. Impax Labs., Inc.*, 356 F.3d 1348, 1357 (Fed. Cir. 2004) ("Prosecution history estoppel, however, is not limited to the applicant's own words, but may embrace as well the applicant's responses to the

examiner's actions. If the patentee does not rebut an examiner's comment or acquiesces to an examiner's request, the patentee's unambiguous acts or omissions can create an estoppel.").

Even today, Auxilium's attempts to broaden its patent coverage have been denied by the Patent Office. In its brief, Auxilium informed the Court that it was pursuing claims that would not be limited to Hsieh enhancers, but rather with a limitation "based on the same specification as the patents-in-suit and recites an enhancer *not limited* to the chemical structure of the enhancer." D.I. 40 at 27 (emphasis is original). Yet, Auxilium failed to inform the Court that since 2009 the Patent Office has rejected this attempt outright as a violation of 35 U.S.C. § 112 on the basis that Gyurik did not "possess the claimed invention," and that the Patent Office will not recognize priority back to the original application. D.I. 61-12, at AUXSJ00000598-601. The Patent Office stated that such a limitation could not be supported by the original specification. *Id.* at AUXSJ00000600.[4] In short, the Patent Office firmly takes the position that such a claim was not part of the invention described in the original Gyurik application.

In total, Auxilium has filed at least seventeen patent applications to date, most of which were filed after Auxilium first sued USL, and some of which remain pending. Taavola Decl. Ex. 1.[5] In the face of the Examiner's rejection over Dudley in view of the Hsieh patent, Auxilium has been unable to broaden its patent coverage to gain allowance of a claim that does not recite one or more of the subset of five Hsieh enhancers. The Patent Office has not allowed Auxilium to gain more than what Gyurik has invented. "[A] patentee should not be able to obtain, under the doctrine of equivalents, coverage which he could not lawfully have obtained from the PTO by

[4] The Examiner noted that the claim now includes "a potentially huge genius inclusive of many different compounds having widely divergent core structures and potential functions. Specifically, the specification does not appear to disclose any compounds which fit this limitation."

[5] "Ex. _" refers to the Declaration of Lars P. Taavola and the exhibits attached thereto, filed contemporaneously herewith.

literal claims." *Wilson Sporting Goods Co. v. David Geoffrey & Asssocs.*, 904 F.2d 677, 684 (Fed. Cir. 1990). "The doctrine of equivalents exists to prevent a fraud on a patent, *not* to give a patentee something which he could not lawfully have obtained from the PTO had he tried." *Id.* (internal citation omitted) (emphasis in original).

B. The common specification contains clear representations and disparaging remarks that not only define the scope of the enhancer limitation but also disclaim USL's co-solvents.

The patents' common specification clearly states that "[t]he enhancer of the present invention is a compound of the structural formula" of a macrocyclic Hsieh enhancer, which is depicted as a chemical structure. D.I. 1, Ex A at col. 6, ll. 23 – col. 7, l. 1 (emphasis added). This statement does not purport to describe "an embodiment" or an "optional" or "preferred enhancer", but simply states that what the present invention "is." Nor does it define a "Hsieh enhancer" in functional terms, but only as a ring structure. Just as the specification in *Augustine Medical* defined the structure of the "self-erecting" limitation, the specification in this case defines the structure of the claimed enhancer. 181 F.3d at 1298.

The patents' common specification in this case invokes the specific properties of the enhancer limitation to distinguish the prior art: the specification clearly distinguishes the claimed enhancer, both structurally and functionally, from the enhancers identified in the Dudley patent. *See Augustine Med.*, 181 F.3d at 1299-1300 ("The specification of the '188 patent thereby invokes its self-erecting structure to distinguish the invention from both convective and conductive prior art thermal blankets."). Here, the specification distinguishes the claimed Hsieh enhancers from the prior art by criticizing the enhancers of the Dudley patent as tending "to irritate the skin" while praising the allegedly inventive Hsieh enhancers as producing "a low level of irritability or no irritability...." *Compare* D.I. 1, Ex. A at col. 3, ll. 65-67 (Dudley and

'919 patent lead to "skin irritation") *with id.* at col. 7, ll. 5-7 (Hsieh enhancers' "low level of irritability or no irritability"). The specification disparages two prior art references teaching *androgen*[6] topical gels – U.S. Patent No. 5,968,919 (on which Gyurik is a named inventor) and the Dudley patent (U.S. Patent No. 6,503,894). *Id.* at col. 3, ll. 51-53. The specification criticizes the prior art androgen gels as inconsistent and lacking emollient properties. *Id.* at col. 3, ll. 60-62. According to the specification, "their use leads to drying of the skin and skin irritation." *Id.* at col. 3, ll. 62-63.

As a solution to the problems of drying of the skin and skin irritation due to lack of emollient properties, the specification introduces a testosterone gel with a special enhancer – a Hsieh enhancer with a macrocyclic structure. *Id.* at col. 6, l. 30 – col. 7, l. 7. According to the specification, this special ingredient does not cause damage to the skin membrane. *Id.* at col. 7, ll. 1-5. And unlike the ingredients in prior art androgen gels, the Hsieh enhancers produce "a low level of irritability or no irritability to the target membrane, and in fact, serve as an emollient." *Id.* at col. 7, ll. 5-7.

It is undisputed that the accused ingredients in USL's formula are three co-solvents all disclosed in Dudley: diisopropyl adipate, methyl laurate and oleyl alcohol. Notably, Auxilium has argued in two petitions to FDA (both of which were filed after commencement of the Related Action[7]) that the properties that it disparaged in the Dudley patent – drying of the skin and skin irritation –are present in USL's formulation. Taavola Decl. Exs. 2-3. In its argument to FDA,[8]

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[6] An androgen is the broad class of compounds that contain testosterone and dihydrotestosterone (DHT). D.I. 1, Ex. A. at col. 1, ll. 19-21.

[7] *Auxilium Pharm., Inc. v. Upsher-Smith Labs., Inc.*, 08-908-SLR (D. Del.)

[8] Auxilium's arguments to FDA about the substantial differences between the formulations and the need for additional studies regarding USL's formulation is hardly congruent with its position before the Court, which is that the USL formulation is "insubstantially different" from the claimed formulation.

Auxilium argued that the presence of diisopropyl adipate, methyl laurate and oleyl alcohol in the USL formulation was the reason why USL should conduct skin irritation studies. Taavola Decl. Ex. 2 at 16. To the FDA, Auxilium claims:

- diisopropyl adipate "is recognized as a skin irritant";
- oleyl alcohol "is also a recognized skin irritant"; and
- esters like methyl laurate "may be irritating to the skin" and "may dry and defat the skin resulting in dermatitis."

Id.

The patents-in-suit all share the same specification. Each of the patents-in-suit therefore identifies the special enhancer as the primary advantage over the prior art that is criticized for irritability. *See Augustine Med.*, 181 F.3d at 1300. Because the specification is common to all claims, the disclaimer in the specification applies to all claims. Just as in *Augustine Medical*, Auxilium should not be permitted to assert the doctrine of equivalents to capture precisely what Gyurik repeatedly criticized in the prior art to distinguish his invention and win patentability.

C. During prosecution of all of the patents-in-suit, Auxilium repeated and extended its disclaimer of non-Hsieh enhancers.

Also as in *Augustine Medical,* the prosecution histories of the patents-in-suit repeat and extend the disclaimers in the specification. Several statements explain the amendments that added specific macrocyclic Hsieh enhancers, and demonstrate the importance of the amendment in distinguishing the Dudley prior art. Statements that recite a limitation to distinguish the claims over the prior art estop the patentee from asserting that the limitation can be met equivalently by the structures found in the art that was distinguished. *Augustine Med.*, 181 F.3d at 1300-01 ("Augustine Medical amended the claims to expressly include a 'self-erecting' limitation and made clear representations of the scope of that limitation to overcome the prior art. Augustine

Medical therefore surrendered during prosecution the coverage it now seeks to reclaim via the doctrine of equivalents.").

It is undisputed that during prosecution of the parent patent (the '968 patent), Gyurik canceled or amended all of the original claims that recited the broad "Hsieh enhancer" limitation to recite the specific Hsieh enhancer Oxa-2-one. D.I. 40 at 7-9. The Applicant made these amendments in response to the Examiner's rejection based on obviousness over the Dudley reference. The prosecution history explains:

> Reference is made to the Examiner's "Interview Summary", mailed June 19, 2007, which indicates the allowability of the claims (that is, the elected method claims) if the claims are amended to define the composition which is referred to in the claims as containing oxacyclohexadecan-2-one (hereafter OXA-2-one), which is the enhancer referred to in dependent claim 62, and testosterone. By virtue of the present claim amendments, all pending claims now define the composition as containing testosterone and OXA-2-one.
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> D.I. 34-1, Ex. 5 at 9.

In addition to the amendment, in the same response, the Applicant submitted three Declarations "which make of record additional evidence of the non-obviousness of the amended claims and, thus, confirm the Examiner's view of the allowability of the method claims which define the use of a composition which includes testosterone and OXA-2-one." *Id.* at 10 (emphasis added). This is a plain admission and notice to the public that the Oxa-2-one limitation was added to distinguish Dudley, and it therefore cannot be met equivalently by the enhancers found in Dudley.

These facts alone limit the scope of at least the claims of the '968 patent, '605-'607 patent, '609 patent, '690 patent '029 patent, and '518 patent. *Augustine Med.*, 181 F.3d at 1300 ("the prosecution history of a parent application may limit the scope of a later application using the same claim term"). Plaintiffs do not dispute that the prosecution history of the '968 patent could restrict the scope of these patents. D.I. 40 at 33.

Auxilium claims that the amendments and the arguments made in the parent application do not restrict the scope of the '608 and '610 patents, since those patents recite additional Hsieh enhancers. *Id.* Auxilium fails to acknowledge, however, that during prosecution of the '608 patent and the '610 patent, Gyurik again focused on the uniqueness of the claimed Hsieh enhancers to distinguish the Dudley reference. Gyurik cited the parent prosecution and the Walters Declaration to overcome the Dudley reference. Gyurik said "[a]ccording to Dr. Kenneth Walters declaration filed in the parent patent and discussed above, the *in vivo* results obtained with TESTIM® were unexpected." D.I. 58-11 at CPEX0115378; D.I. 59-6 at CPEX0116069. In each case, Gyurik submitted test data to show that the formulations with the additional specific macrocyclic enhancers were very similar *in vitro* when compared with TESTIM®. D.I. 58-11 at CPEX0115378-79; D.I. 59-6 at CPEX0116068-69. It was Gyurik's "position that because the tested example formulations within the scope of the present claims yielded equally unexpected and surprising results as TESTIM®, these claims are not obvious over Dudley et al. (U.S. Patent No. 6,503,894) in view of Hsieh (U.S. Patent No. 5,023,252)." D.I. 58-11 at CPEX0115378-79; D.I. 59-6 at CPEX0116068-69. In each case, the Examiner rejected the pending claims, since they were not the formulas tested or disclosed. D.I. 58-12 at CPEX0115409-10; D.I. 59-7 at CPEX0116101-02. Gyurik amended the claims to recite specifically the macrocyclic compounds he had tested. D.I. 58-12 at CPEX0115421; D.I. 59-7 at CPEX0116115. Once again, the Applicant emphasized the limitation to macrocyclic enhancers added by amendment to distinguish the claimed combination over the Dudley prior art.

As the Examiner recognized, "Hsieh teaches a new class of enhancers" that were not taught by Dudley. D.I. 40 at 6; D.I. 50 ¶ 130. And the Applicant, when confronted with an obviousness rejection over Dudley in view of the Hsieh patent, stated "[a]mong all of the

hundreds of enhancers (perhaps thousands) disclosed by Dudley et al., there is no reference whatsoever to a Hsieh enhancer...." D.I. 34-1, Ex. 1 at 24-25. The message to the Examiner, and to the public, could hardly be clearer – the Gyurik invention was not to be found in the disclosure of Dudley, because Gyurik's invention requires Hsieh enhancers.

The representations distinguishing the prior art that accompanied the amendment are a prosecution disclaimer, just as in *Augustine Medical*. The relevance of the amendment in this case is that it provides context to understand the express disclaimer that accompanied the amendment – it further shows that the patentee explicitly relied on the presence of a particular Hsieh enhancer to distinguish his invention from prior art testosterone gels that used non-Hsieh enhancers. Having made the amendment and explained its importance, the patentee is estopped from recapturing what it distinguished. In sum, during prosecution of the patents-in-suit, Gyurik amended his claims to expressly include the specific Hsieh enhancer limitations and made clear representations of the scope of that limitation to overcome Dudley. Therefore, Auxilium surrendered during prosecution the coverage that it now seeks to reclaim via the doctrine of equivalents. *See Augustine Med.*, 181 F.3d 1299-1301.

D. Auxilium cannot use the doctrine of equivalents to extend its patents to cover new and novel solutions to the same problem.

For the purposes of equivalents, Auxilium surrendered the entire teachings of the Dudley reference regarding enhancers.[9] As noted by the Examiner during prosecution of the '518 patent, "Dudley is not limited by its example [Androgel] but good for all that it teaches." D.I. 60-14 at

[9] This surrender does not imply that no formulation that includes a Dudley enhancer can be found to infringe the claims of the patents-at-issue as long as they *also* contain one of the five claimed macrocyclic Hsieh enhancers. Contrary to Auxilium's protestations of a "nonsense" result, D.I. 40 at 27, the surrender means that propylene glycol cannot be an *equivalent* of a Hsieh enhancer in a formula that lacks the claimed enhancers, but it can be included in a formulation that includes a claimed enhancer and otherwise meets the limitations of the claim.

AUXSJ00001194-95. Auxilium cannot reasonably claim that its disclaimer is limited solely to the enhancer isopropyl myristate, or even to the individual enhancers listed in Dudley. The scope of the estoppel is larger, because the patentee distinguished the claimed Hsieh enhancers from all non-Hsieh enhancers. *Augustine Med.*, 181 F.3d at 1299 ("the prior art may aid in determining the scope of an estoppel.").

To determine the scope of the estoppel "a close examination must be made as to, not only what was surrendered, but also the reason for such a surrender." *Southwall Techs. Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1580 (Fed. Cir. 1995) (citation omitted). This inquiry is a matter of law for the Court, and not an issue that can be raised as an alleged factual dispute to defeat summary judgment. *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1254 (Fed. Cir. 2000).

In distinguishing Dudley, Gyurik made specific statements that the claimed Hsieh enhancers are different from the Dudley enhancers. D.I. 34-1, Ex 1 at 19. Gyurik's formulation including the Hsieh enhancers purportedly solves certain problems of the prior art – skin irritation and emulsion properties. Gyurik also specifically relied on the claimed enhancers and test data associated with those enhancers. D.I. 40 at 24. Thus, an examination of both the nature of and the reason for Auxilium's disclaimer of the Dudley enhancers demonstrates that the Gyurik surrendered all Dudley enhancers individually or in combination.

Moreover, the prior art expressly teaches that combining enhancers was known to those skilled in the art. D.I. 51 ¶ 136. When Gyurik was evaluating the landscape of testosterone gels, he knew that combining enhancers was a known approach in the art. In fact, when it served his purposes, Gyurik chose to describe and claim combinations of the specific Hsieh enhancers that he tested and claimed (*see, e.g.*, D.I. 1, Ex. E, '608 patent claim 1 – "(B) about 0.5 to about 25%

of a macrocyclic enhancer selected from the group...*and mixtures thereof*" (emphasis added)), or combinations of Hsieh enhancers and known enhancers (*see* D.I. 1, Ex. A at col. 8, l. 65 – col. 9, l. 3). During prosecution of each of the patents, Gyurik further acknowledged prior art references that taught combinations of enhancers:

- 5,731,303 (Hsieh) – "The skin-treating compound(s) is used in conjunction with an enhancer which is a compound within the scope of Formula I above. A plurality of enhancers can be used. Additional improvements in the qualities of the skin are achieved by the use of the enhancer(s) in combination with the skin-treating compound"

- 6,319,913 (Mak) – "Formulations comprised of combinations of ingredients of the same type instead of only one ingredient of that type, such as using a combination of two solvents instead of just one solvent, have been reported to lessen irritation without lowering drug permeation. This approach has also been applied to penetration enhancing agents."

- 7,214,381 (Carrara) – "To be accepted, a permeation enhancer or a combination thereof should have the ability to enhance the permeability of the skin for the drug, should be non-toxic, non-irritant and non-sensitizing on repeated exposure. . . . Therefore, the usefulness of a particular compound(s) or mixture thereof as a permeation enhancer must be carefully analyzed and demonstrated by empirical work."

  (Emphases added.)

Auxilium is incorrect when it argues that the estoppel is limited to the specific embodiments expressly taught in Dudley. D.I. 40 at 19, 26. This is not the law. The Federal Circuit has repeatedly rejected the argument that "prosecution history estoppel is limited only to the embodiments shown in the prior art." *Southwall*, 54 F.3d at 1581. Rather, the "limits imposed by prosecution history estoppel on the permissible range of equivalents can be broader than those imposed by the prior art." *Id.* Here, Auxilium expressly distinguished and criticized "non-Hsieh" enhancers, and should be held at least to that surrender. Moreover, Auxilium distinguished the "hundreds perhaps thousands" of enhancers in Dudley and should be held to that surrender. Where it was well-known in the acknowledged prior art that enhancers can be combined, Auxilium should not be heard now to take back its disclaimer simply because USL used a

combination of the enhancers listed in Dudley. The only reasonable construction is that Auxilium disclaimed the "hundreds perhaps thousands" of non-Hsieh enhancers in Dudley whether they are used alone or in combination.

II. While Auxilium attempts to raise irrelevant factual disputes or impermissible issues using declarations, these declarations admit all of the material facts required to determine estoppel.

Auxilium filed declarations with its brief in an attempt to overwhelm the record in factual minutiae. Most of the assertions in the declarations are not material to resolution of summary judgment, because the declarations are largely immaterial, and admit the material facts. Declarations introduced for purposes of litigation cannot contradict the prosecution disclaimer that is evident from the intrinsic record, which speaks for itself here. The Federal Circuit has stated that expert declarations, like Dr. Friend's declaration, cannot create a question of material fact regarding the objective inquiry regarding disclaimer. *Bayer AG,* 212 F.3d at 1254 ("testimony as to what a reasonable competitor would conclude from the prosecution history cannot create a genuine issue of material fact so as to bar summary judgment. Such testimony is only a tool, which the judge can use at his or her discretion, to aid in the legal determination of prosecution history estoppel.").

The proper inquiry is an objective standard as to "whether a competitor would reasonably believe that the applicant has surrendered the relevant subject matter." *Id.* at 1252 (citation omitted). Plaintiffs attempt to create new law by stating that "[a]rgument-based estoppel applies only when a *skilled artisan,* viewing the question from the perspective of a competitor in the marketplace, would believe that the patent applicant surrendered the relevant subject matter" D.I. 40 at 26. For this proposition, Plaintiffs cite *Cordis Corp. v. Medtronic AVE, Inc.*, 511 F.3d

1157, 1177 (Fed. Cir. 2008). *Cordis* does not stand for the proposition and, in fact, does not even reference one of ordinary skill in the art at the cited page.

Auxilium's arguments regarding unforeseeability and tangentiality are also irrelevant to disclaimer in this case. *Conoco*, 460 F.3d 1363-65. While unforeseeability and tangentiality could rebut estoppel that is based on amendment alone, the express disclaimer based on the specification, claims and the distinctions over the prior art in the file histories of the patents-at-issue cannot be rebutted based on unforeseeability or tangentiality. *Id.*

In addition, the Declarations are misdirected regarding unforeseeability and tangentiality. As a matter of law, the non-cyclic enhancers described in Dudley and comprising the alleged "enhancer system" are foreseeable. It is undisputed that the "enhancer system" ingredients were disclosed in the Dudley reference, and that combining enhancers to achieve a result was known in the prior art. As held by the *Festo XIII* court *en banc*: "An equivalent is foreseeable if one skilled in the art would have known that the alternative existed in the field of art as defined by the original claim scope, even if the suitability of the alternative for the particular purposes defined by the amended claim scope were unknown." *Festo XIII*, 493 F.3d at 1382.

Here, the ingredients were disclosed in the prior art in the field of the invention, as was the possibility of combining them, and they are therefore foreseeable as a matter of law. "Foreseeability does not require that the accused infringing product or process be foreseeable, nor that any equivalent exist at the time; rather foreseeability only requires that one of ordinary skill in the art would have reasonably foreseen the proposed equivalent at the pertinent time." *Honeywell Int'l, Inc. v. Hamilton Sunstrand Corp.*, 523 F.3d 1304, 1314 (Fed. Cir. 2008); *see also, Duramed Pharms, Inc. v. Paddock Labs., Inc.*, 644 F.3d 1376, 1380-82 (Fed. Cir. 2011); *Schwartz Pharma, Inc. v. Paddock Labs., Inc.*, 504 F.3d 1371, 1377 (Fed. Cir. 2007).

Auxilium's argument that its amendment to the five specific macrocyclic enhancers is "tangential" to patentability is simply untethered to the facts. The penetration enhancer limitation and the teachings in Dudley were *central* to the prosecution. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1369 (Fed. Cir. 2003) ("Festo X") (an amendment "made to avoid prior art that contains the equivalent in question is not tangential; it is central to the allowance of the claim."). Throughout the prosecution, Gyurik provided specific test results to overcome the obviousness rejection based on Dudley. Auxilium claims that the amendments were to "satisfy the Examiner's continued insistence that the claims be commensurate in literal scope with the data showing unexpected results," and implies that the amendments were not used to overcome Dudley. DI. 40 at 24 (citing D.I. 50 ¶¶ 209-211). As the Examiner stated "this is not entirely accurate." As discussed above, page 6, the amendments were made to overcome Dudley and the patents were not granted solely based on the showing of unexpected results. *See* D.I. 60-14 at AUXSJ00001194-95.[10] To say that the claims were *not* amended in response to the *prima facie* obviousness rejection over Dudley is simply preposterous. That was the *only* reason for the amendment and for the showing of unexpected results.

Moreover, the Court should not even consider the Friend Declaration. The determination of whether an amendment is tangential is based on "the patentee's objectively apparent reason for the narrowing amendment" and is based on the intrinsic record alone. *Festo X*, 344 F.3d at 1369-70. Dr. Friend, throughout his declaration, attempts to impart additional evidence by providing subjective, hindsight, litigation-driven and wholly unpersuasive reasons for the amendments and arguments – that Gyurik was financially compelled to drop his resistance to amending the claims. D.I. 40 at 8 (citing D.I. 50 ¶ 193). Such extrinsic subjective evidence is

[10] Auxilium's own patent prosecution counsel plainly admitted as much at his deposition: D.I. 27 at 7.

contrary to the public notice function of the patent record. *Festo X*, 344 F.3d at 1370. The record is unambiguous.

To be clear, the Court need not reach Auxilium's incorrect arguments about unforeseeability and tangentiality because the Court can and should dispose of the entire case on the disclaimer branch of the estoppel analysis. Foreseeability and tangentiality are simply irrelevant to the limits on the doctrine of equivalents in this case.

CONCLUSION

Auxilium does not dispute the material facts that are dispositive: its specification, claims, and file history all emphasize the macrocyclic Hsieh enhancers to overcome the known enhancers of the prior art, including non-cyclic enhancers described in Dudley and present in the USL formulation. Based on amendments and arguments during prosecution, Auxilium cannot in litigation extend its patent coverage to include USL's formulation that lacks the recited Hsieh enhancers. As recognized throughout the case law, the doctrine of equivalents is to extend to insubstantial changes. USL's formulation is not an insubstantial change.

The *Wrigley* doctrine also compels the result here. *W.M. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 683 F.3d 1356, 1366 (Fed. Cir. 2012). Gyurik only claimed to invent a formulation with a very specific subset of macrocyclic Hsieh enhancers. He only obtained allowance of the patents by providing test data for specific formulations to overcome *prima facie* obviousness. USL's structurally different non-cyclic compounds[11] were known to Gyurik, as was the fact that enhancers could be combined in a formulation. Auxilium argues that *Wrigley* was

[11] Auxilium also attempts to argue that *Abraxis Bioscience, Inc. v. Mayne Pharma (USA) Inc.*, 467 F.3d 1370 (Fed. Cir. 2006) controls; however, as Auxilium acknowledges, the alleged equivalent in *Abraxis* was "structurally similar." Auxilium conveniently ignores the readily apparent structural differences present in this case – the claimed Hsieh enhancers are cyclic (in fact, macrocyclic) compounds (D.I. 50 ¶ 131), while the components of the alleged "enhancer system" are non-cyclic compounds. *Id.* ¶ 166.

dependent on the fact that the inventors learned of the gum components "during the same sales call, and they were told that the two compounds were appropriate for the same uses." D.I. 40 at 35 (*citing Wrigley*, 683 F.3d at 1366). This distinction is erroneous, as it would turn an objective inquiry into a subjective one. But even so, Gyurik knew that the enhancers in Dudley were appropriate for use with testosterone: he referenced and disparaged the Dudley patent in his own specification. He drafted the claims narrowly to recite certain Hsieh enhancers, not a broader category of enhancers. *See Wrigley*, 683 F.3d at 1366. The undisputed evidence demonstrates that his invention includes only compositions that include Hsieh enhancers, and that his invention does not include compositions that do not. Therefore, USL respectfully requests judgment of non-infringement.

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